UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/698,213	10/30/2000	James D. McInnch	04983.0220.00US00/38-10(1	6072

28381 7590 07/30/2002

ARNOLD & PORTER
IP DOCKETING DEPARTMENT; RM 1126(b)
555 12TH STREET, N.W.
WASHINGTON, DC 20004-1206

EXAMINER	
SHEINBERG, MONIKA B	
ART UNIT	**PAPER NUMBER**
1631	16

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/698,213	Applicant(s) MCININCH, JAMES D.
	Examiner Monika B Sheinberg	Art Unit 1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *17-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16 and 41-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-44* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-16 and 41-44) in Paper No. 14, filed: 10 May 2002, is acknowledged. Claims 41 and 44 were omitted from the previous office action, however have now been appropriately included in Group I. Applicant's traversal of the restriction is on the ground(s) that all the groups are related in that they are directed to the probability determination for one or more states for a nucleotide in a nucleic acid sequence. This is not found persuasive because applicant clearly stated within the specification on page 19 (lines 17-21) that the methods are independent of each other, and have the ability to include other methods that perform their internal steps of methodology than the ones recited. In addition, Group I does not require a key step of methodology, a summation of probabilities, as do the other groups. The requirement is still deemed proper and is therefore made FINAL.

Claims 17-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Drawings

Drawings filed 10 May 2002 are acknowledged and accepted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and

reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant application fails to provide guidance to one of ordinary skill in the art for determining whether a probability of a state of a nucleotide is "capable of accepting a bias" as seen in claim 7, line 10. The specification does not provide or suggest what is the determinant for bias acceptance thus not enabling one of ordinary skill in the art to know what requirements must be met to qualify for acceptance. Page 18 (lines 16-17) discloses that the bias is utilized to "alter" the probability yet does not teach bow it is decided when the probability will "accept"/ Pages 24-25 disclose the use of the bias function for both coding and non-coding sequences yet not a condition when a bias was not accepted. None of the examples provide a description of how to determine a probability's capability to accept a bias. The prior art does not teach determining bias acceptance. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of descriptive working examples in the specification, and the unpredictability of determining a probability's capability to accept a bias, the specification, as filed is not enabling for determining a probability for a state of a nucleotide when bias acceptance is not enabled as claimed.

Claims 1-16 and 41-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the following:

Initial oligonucleotide probability	p. 21, equation I,
Transition probability	p. 22, equation II,
Nucleic acid sequence probability	p. 23, equation III,
Probability for each nucleotide state	p. 24, equation IV, and

Bias function at 0.0, 0.05, 0.95, and 1 pp. 24 and 47;

the specification does not reasonably provide enablement for any method of computation for determining the above probabilities nor determining how much of a bias is to be used aside from the numbers indicated above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPA 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The instant application fails to provide guidance to one of ordinary skill in the art for generating the probability values of the following by any other means than by the equations indicated below:

Initial oligonucleotide probability p. 21, equation I,
Transition probability p. 22, equation II,
Nucleic acid sequence probability p. 23, equation III, and
Probability for each nucleotide state p. 24, equation IV;

nor determining a bias other than at the following:

Bias function at 0.0, 0.05, 0.95, and 1 pp. 24 and 47.

The specification does not provide or suggest what any other substitutable methods of computation could be for the above probability determinations thus not enabling one of ordinary skill in the art to know what calculations to perform. While the specification provides some guidance for a method of determining a probability value for the above listing using the particular equations or values disclosed, the specification does not provide guidance for a method

of determining the probability value by any other means. The specification does not provide any guidance on the determination of how much bias is to be utilized. For example the specification does not specify how to "bias the state probabilities in favor of the coding states" as recited in lines 25-26; how to determine the amount to create "favor" is not disclosed. Nowhere in the specification are the limitations of any biases such as "greater than 1.1" (claims 6 and 16) disclosed other than the values 0, 1, 0.05 and 0.95. The specification does not provide working examples of the methods described using any other means of computing the described probability values. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of descriptive working examples in the specification, and the unpredictability of generating probability values, the specification as filed is not enabling for any method of determining the listed probability values as claimed. The instant application is only enabled for the following computational means:

Initial oligonucleotide probability	p. 21, equation I,
Transition probability	p. 22, equation II,
Nucleic acid sequence probability	p. 23, equation III,
Probability for each nucleotide state	p. 24, equation IV, and
Bias function at 0.0, 0.05, 0.95, and 1	pp. 24 and 47.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 and 41-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7, 8 and 41-44 are vague and indefinite due to the lack of clarity in the term "based upon" (i.e. claim 1, line 8). It is unclear as to what are the metes and bounds of the parameters that determine how much basis is included upon the determinations. Claims 2-6 and 9-16 are also indefinite due to their dependency from claims 1 and 8.

Claims 4 and 13 recite the limitation "the middle nucleotide" in lines 1 and 2 respectively. There is no antecedent basis for this limitation in the claims.

The term "capable" is claim 7 is a relative term that renders the claim indefinite. The term "capable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 1, 7 and 43 are vague and indefinite due to the lack of clarity in the steps of methodology. For example, claim 1 in steps (a) and (b) determine two different probability values that are ignored in step (d), the goal action step of determining the probability for one or more states of a nucleotide. Claims 2-6 are also indefinite due to their dependency from claim 1.

Claims 3 and 11 are vague and indefinite due to the lack of clarity in the following terms: f, S P_f, P_i *and* Φ. It is unclear as to what are the metes and bounds of these terms.

Claims 8 and 44 lack clarity in step (c) due to the claim language "determining a probability **for** said window **for** said nucleotide" lines 7 and 9 respectively. Claims 9-16 are also indefinite due to their dependency from claim 8.

Claims 6, 15 and 16 are vague and indefinite due to the numbers "0.0", "0.9", "1.1", "75" and "125" lacking any descriptive units. For example, "75" and "125" of claim 15 lack clarity as to whether the numbers indicate lengths in terms of nucleic acids or codons, and so forth.

Claim 15 is vague and indefinite due to the lack of clarity in the terms "of about" and "to about". It is unclear as to what extent of "about" is intended; how close to 75 or 125 is about indicative of; how close is close.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 5, 7-9, 12, 13, 15 and 41-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Borodovsky et al (*Computers Chem.*, 1993).

Due to claims 1, 7, 8 and 41-44 not requiring a limited bias, the reference anticipates the instant invention whereupon "a bias of 1 for all coding states" (p. 24, last sentence) is applied. The specification discloses in the bridging paragraph of pages 24-25, the determined probability to be "unaffected" (p. 25, line 1). As such, the probability determinations are equal with or without bias. Borodovsky et al teaches a computer-implemented method (GENMARK) for determining different state probabilities of a nucleotide in a sequence using non-homogeneous Markov models, including initial and transitional probabilities as recited in claims 1, 7, 8 and 41-48. The reference analyzes a nucleotide fragment "*F*"(p. 128, 2nd column, 3rd paragraph) of the nucleic acid sequence of interest as recited in claims 5 and 12; sequentially analyzes through repetition, "every fragment *F* found in the window" (p. 129, 2nd column, 1st paragraph) as recited in claims 9, 42 and 44 with reference to the middle nucleotide of the window or section of the fragment under analysis as recited in claims 4 and 13. Borodovsky et al demonstrates the method of claims 8, 42 and 44, utilizing varying window sizes of 48-94 nucleic acids in length; this also anticipates the indefinite limitation of a widow length "of about 75 to about 125" in claim 15. The GENMARK method as a program teaches the "program storage device readable by machine" of claims 43 and 44. Thus Borodovsky et al anticipates the instant claims with a bias of 1 for the coding states.

Conclusion

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

July 26, 2002
Monika B. Sheinberg
Art Unit 1631

MBS

Marianne P. Allen

MARIANNE P. ALLEN
PRIMARY EXAMINER
GROUP 1600
AU1631